

**UNITED STATES DEPARTMENT OF COMMERCE****Patent and Trademark Office**Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231**HL**

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

09/029,830 03/10/98 KASK

P F618130USD

JACOBSON PRICE HOLMAN & STERN
400 SEVENTH STREET NW
SUITE 600
WASHINGTON DC 20004

HM12/0708

EXAMINER

GARCIA, M

ART UNIT	PAPER NUMBER
----------	--------------

1618

7

DATE MAILED:

07/08/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/029,830	Applicant(s) Kask
	Examiner Maurie E. Garcia, Ph. D.	Group Art Unit 1618

Responsive to communication(s) filed on _____.

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire THREE month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 1-28 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 1-28 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 6

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

KEITH D. MACMILLAN
PRIMARY EXAMINER

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Drawings

2. This application has been filed with informal drawings, which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.52. See attached PTO-948 for the details of these objections. Correction of the noted defects in the drawings can only be deferred until the application is allowed by the examiner.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 3, 5, 6, 11, 12, 13, 15-18, 20-23, 25, 26 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
- A. In claim 3 the term "units" is indefinite. It is not clear what the metes and bounds are of this term and hence, what constitutes the claimed invention. Therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. In reviewing the specification, the term "units of sample" is defined on pages 3-4 but it is defined so broadly as to still render the claim indefinite. The term is confusing, since from the definition in the specification it would seem that "units" are subparts of a sample but subparts could be construed to mean monomers of a polymer, or different molecular components of an aggregate or a metal and its chelant, etc. It is additionally unclear what is meant by "samples having units" – is this one sample with many units, many samples with one unit or many samples with many units? Also, are the units all the same or different? Since both of the terms are plural, it is difficult to ascertain the meaning of this phrase.
- B. In claim 3 the term "centers" is indefinite. It is simply unclear what is meant by this term and a definition could not be found in the specification.
- C. Claim 5 lacks antecedent basis for the term "species". This term is not mentioned in claim 1, from which claim 3 depends.
- D. Regarding claim 6, the phrase "in particular" renders the claim indefinite. A broad range or limitation together with a narrow range or limitation that falls within the

broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.

Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

E. In Claim 11 the phrase "the sample is actively transported" is indefinite. It is unclear what this term means, especially since the phrase "being actively transported into and out of said measurement volume" precedes the phrase in question. Are these two phrases supposed to be identical in meaning? The difference between them is unclear.

F. Regarding claim 12, the phrases "in particular" and "preferably" render the claim indefinite because it is unclear whether the limitation(s) following the phrases are part of the claimed invention. See MPEP § 2173.05(d). See also Rejection D above.

G. In claim 13 the term "optionally" is indefinite because it is unclear what applicant intends. If an element is truly optional, i.e. its presence is not necessary for attainment of the result that is the object of the invention, then recitation of such should not be made in the claims. Otherwise, the examiner suggests that the variant should be written as a

dependent claim using “further comprising” language. It is also unclear exactly how the confocal microscope set-up is supposed to be used in the method.

H. Claims 15-18 are indefinite because they lack antecedent basis and/or are improperly dependent. These claims recite terms that are not mentioned in claim 1, from which they all depend. They appear to be dependent on the wrong claim, as they mention terms that are found in other dependent claims and the current dependency is confusing. For example, claim 15 mentions fluorescence, claim 16 a spatial brightness function and optical set-up, claim 17 a pinhole and a microscope and claim 18 an incident laser beam.

I. Claims 20-21 are indefinite because they lack antecedent basis and/or are improperly dependent. These claims recite the term “said distribution”, which is not mentioned in claim 1 from which they both depend. They appear to be dependent on the wrong claim; the current dependency is confusing.

J. Regarding claim 22, the phrase “in particular” renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). See also Rejection D above.

K. Claim 23 lacks antecedent basis for the term “equipment”. Equipment is not mentioned per se in claim 1, from which claim 23 depends. The term “equipment” is additionally indefinite since it is unclear what equipment is being referred to – is this meant to indicate the detection means?

L. Regarding claims 25 and 26, the phrase “preferably” renders the claims indefinite because it is unclear whether the limitation(s) following the phrases are part of the claimed invention. See MPEP § 2173.05(d). See also Rejection D above.

M. Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are as follows: how to use the method of claim 1 in the recited processes/techniques, especially in techniques such as diagnostics and screening.

5. It should be noted that in art rejections that follow, the examiner is interpreting the claims in their broadest sense as written. Since it is unclear what the meaning of “units” is (see Rejection A above), this term is taken to mean any subpart of a sample that can emit, scatter or reflect radiation (i.e. fluorescent or luminescent molecules).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-5, 8-14, 19 and 22-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Nie *et al* (Anal. Chem., 1995, Vol. 67, pp. 2849-2857).

Nie *et al* teaches a method very similar to the claimed method. Detection of single molecules in solution is performed, with the molecules in question being biomolecules or dyes (see page 2851). Confocal fluorescence microscopy is used for the detection and concentration measurements (see page 2852). Volumes are determined by the optics of the set-up (see Figure 1) which is very similar to that recited in the instant claim 13. Molecules with multiple binding sites are discussed and the molecules are in motion during the measurement (page 2853 and Figure 5). The molecules are arranged on a glass slide (two-dimensional carrier).

8. Claims 1-6 and 8-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishikawa *et al* (EP 0601714 A1, Hamamatsu Photonics K.K. Published: 6/15/94).

Ishikawa *et al* also teaches a method very similar to the claimed method (see Abstract and Figure 2). Fluorescence is used to confirm the presence and concentration of molecules, especially biomolecules. The set-up is very similar to that recited in the instant claim 13 (see Figures 1-2 and page 5). The detection of molecules is described on pages 5-9, in particular the detection of biotin-avidin complexes (page 7, lines 35-44).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable Nie *et al* (Anal. Chem., 1995, Vol. 67, pp. 2849-2857) in view of Nag (US 5,763,585 Issued: 6/9/98, Filed: 4/14/94).

Nag teaches “his tags” and conjugates thereof with Ni-NTA (see columns 12-13).

These complexes are well known in the art. Nag lacks the teaching of detecting these complexes using the fluorescent methods of the instant invention. However, Nie *et al* teaches a method for analyzing biomolecules in such a manner; this system would work with any complex. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to detect the conjugates of Nag using the method of Nie *et al*. A person of ordinary skill in the art would have been motivated to use the method of Nie *et al* in order to be able to detect the compounds at very low concentrations.

Status of Claims

11. No claims are allowed.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Friday from 9:30 to 6:00.

13. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams, Ph.D., can be reached on (703) 308-0570. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



KEITH D. MACMILLAN
PRIMARY EXAMINER

Maurie E. Garcia, Ph.D.
July 6, 1999